Final Report for AOARD Grant FA2386-12-1-4090

"Sensory systems neuroscientists face one fundamental puzzle on their desks: How primary sensory cortex balances the weights on extrinsic and intrinsic sources of information?"

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Name of Principal Investigators (PI and Co-PIs): Sang-Hun Lee (PI, SNU), Randolph Blake (co-PI, Vanderbilt university)
- e-mail address : visionsl@snu.ac.kr
- Institution : Seoul National University
- Mailing Address : Rm 647 Bldg 220 Seoul National University, 1 Gwanak-ro Gwanak-gu, Seoul 151-742, South Korea
- Phone : +81-2-880-9129
- Fax : +81-2-871-9129

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Abstract: Using functional magnetic resonance imaging (fMRI) and spectroscopy (fMRS), our studies conducted a series of experiments with aims of revealing the architecture of functional connectivity among local gray-matter tissues within V1 and the mechanisms of task-dependent top-down modulations of V1. We confirmed that (1) fMRS measurements in human a 3T MRI scanner are sensitive enough to detect task-driven attentional modulation in medial prefrontal cortex (mPFC) and that (2) Noise correlations are relatively high for the voxel pairs whose RFs fall upon the same polar angle axis or the same eccentricity axis. Currently, encouraged by these positive pilot results, we are planning to conduct further experiments, wherein Cho signals in V1 and the basal forebrain area were measured while top-down factors such as 'decision uncertainty' are manipulated as an independent variable.

Introduction: During the decades immediately following Hubel and Wiesel's seminal discoveries, research focused on predicting responses of sensory neurons to simple visual features, and from that work emerged a standard model based on linear spatiotemporal filtering . More recently, however, the standard model has faced new challenges imposed by the discovery of modulatory influences flowing into individual neurons either from other neighboring neurons, or from other parts of the brain. These influences have led to new proposals about how exogenous and endogenous factors interactively shape responses within early visual cortex, including primary visual cortex (V1). Given this contemporary view of V1 activity, our research is trying to answer a fundamental question: How do V1 neurons maintain high-fidelity sensory signals carried within the afferent currents while, concurrently, their activity levels are modulated either by local currents flowing from neighboring neurons co-activated by sensory input ('functional connectivity') or by top-down currents from high-tier brain regions engaged during an ongoing perceptual task ('top-down modulation')? Using functional magnetic resonance imaging (fMRI) and spectroscopy (fMRS), our studies aim at revealing the architecture of functional connectivity among local gray-matter tissues within V1 and the mechanisms of task-dependent top-down modulations of V1.

Experiment:

1. Functional MRS experiment

Hypothesis. "Whether fMRS measurements in human a 3T MRI scanner are sensitive enough to detect task-driven attentional modulation in medial prefrontal cortex (mPFC)?"

Independent variable.
- Baseline condition: Instructed button press task

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14. ABSTRACT

Using functional magnetic resonance imaging (fMRI) and spectroscopy (fMRS), our studies conducted a series of experiments with aims of revealing the architecture of functional connectivity among local gray-matter tissues within V1 and the mechanisms of task-dependent top-down modulations of V1. We confirmed that (1) fMRS measurements in human a 3T MRI scanner are sensitive enough to detect task-driven attentional modulation in medial prefrontal cortex (mPFC) and that (2) Noise correlations are relatively high for the voxel pairs whose RFs fall upon the same polar angle axis or the same eccentricity axis. Currently, encouraged by these positive pilot results, we are planning to conduct further experiments, wherein Cho signals in V1 and the basal forebrain area were measured while top-down factors such as ?decision uncertainty? are manipulated as an independent variable.

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- Attention condition: Target position discrimination task

Stimulus and task. A sinusoidal grating, which was embedded in white-and-pepper noise dots confined within a square region, was presented unpredictably either in the left hemifield or in the right hemifield over several minutes while a subject was fixating at the center of projector screen (Fig 1). In the baseline (preR and postR) conditions, the subject was simply asked to press one of two buttons depending on the color of the fixation dot. In the experimental (AT) condition, the subject judged which square region (left or right) the sinusoidal grating appeared and pressed a button accordingly ('two-alternative-forced-choice' (2AFC) task). The two conditions were identical except for the difference in task.

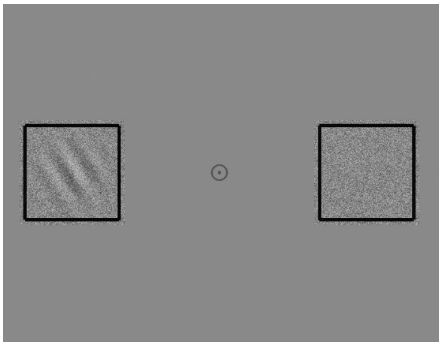

Figure 1. Stimuli and task of the fM RS experiments

Localization of regions of interests.

- mPFC: By contrasting fMRI measurements from the whole brain while the subject was performing the baseline and attentional tasks alternatingly, we defined the area mPFC by delineating a cluster of voxels who showed significant modulations (Fig 2a,b).
- M1: By contrasting fMRI measurements from the whole brain while the subject was performing the button press and resting tasks alternatingly, we defined the primary motor area (M1) by delineating a cluster of voxels who showed significant up-state modulations (Fig 2c,d).
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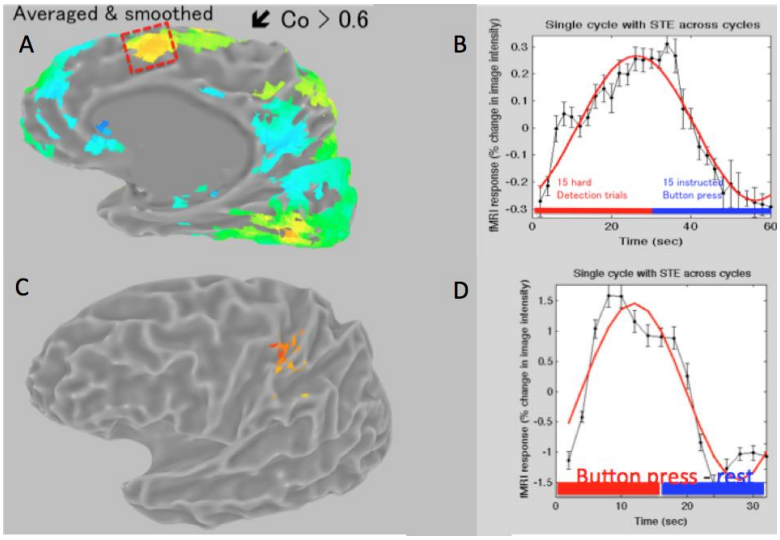

Figure 2. Regions of interest, mPFC(a,b) and M1(c,d)

Dependent variable. Power modulation amplitudes (arbitrary unit) of chemical shift/mm matched to Choline (Fig. 3)

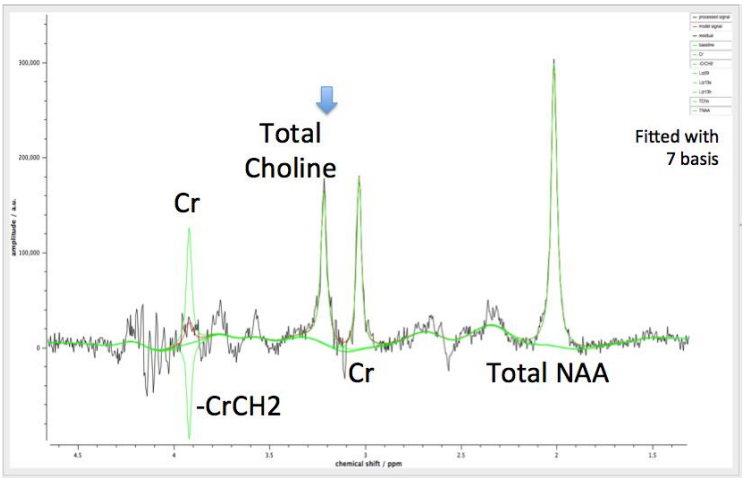

Figure 3. Profile of amplitude as a function of chemical shift per ppm

Prediction. "If fMRS measurements are sensitive enough to detect cholinergic neuromodulation induced by attentional modulation, the Choline amplitude (indicated by the arrow in Fig. 3) will be significantly higher in the attention condition than in the baseline condition.

Results. The prediction was supported by statistical analysis. In addition, NAA (N-Acetyl Aspartate) and Cr (Creatine) were also significantly and positively modulated by the attention task.

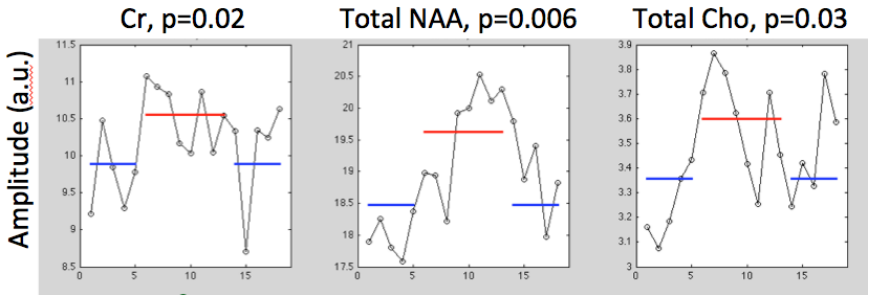

Figure 4. Attentional modulation of fMRS in mPFC across scan runs. Red (attention runs) versus Blue (baseline runs)

2. Noise correlation and resting-state fMRI experiments

Hypothesis. "Whether driven and spontaneous fluctuations in fMRI measurements exhibit any visuotopic anisotropy in moment-to-moment correlation between local sites in primary visual cortex?"

Experimental variables. States (Driven vs Spontaneous) x Geometric relationship between sites (spiral angle, -90 (radial)~-45 (spiral) ~ 0 (radial) ~ +45 (spiral) ~ +90 (radial) (Fig 5)

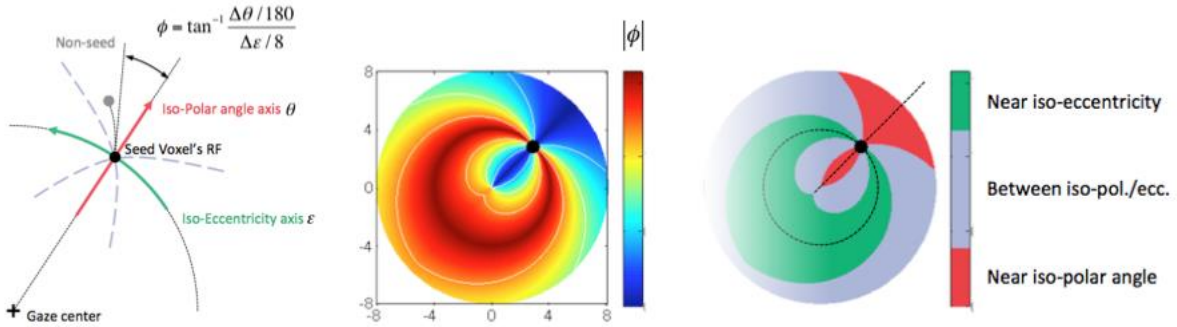

Figure 5. Definition of spiral angle between sites in visuotopic space

Methods. V1, V2, and V3 were localized from five subjects using conventional retinotopic mapping

experiment (Fig. 6a). The locations of the receptive field for individual voxels ($2 \times 2 \times 2mm^3$) from those areas were carefully estimated by 2D Gaussian receptive field model (Fig. 6b). The anatomical distances for each voxel pairs were estimated by searching for the shortest paths along the pial and/or white matter surface boundaries segmented from high resolution ($1 \times 1 \times 1mm^3$) T1 image (Fig. 6c).

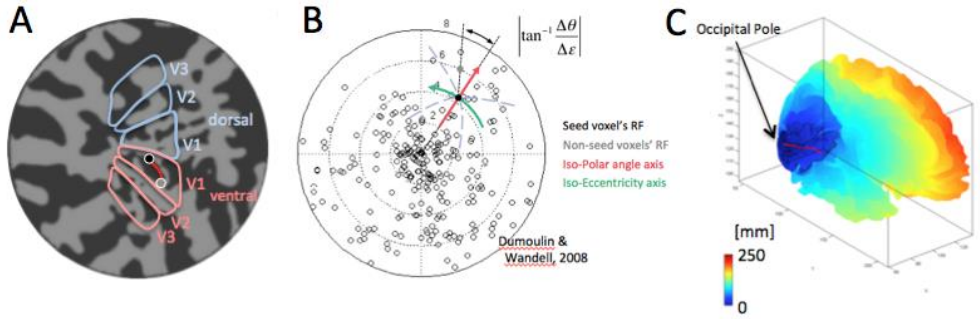

Figure 6. Definition of visual area boundaries, individual voxels' receptive fields and cortical surface distance between a pair of voxels

In the main experiment, full-field patch visual stimuli whose orientation or spatial frequency content is monotonically modulated were repeatedly presented while subjects were asked to perform the fixation task (Fig. 7). Noises for individual voxels were defined by the time courses of deviations from their own across-trial average responses, and noise correlations were defined voxel pairwise by the Pearson's correlation (Fig. 8). Noise correlations were also obtained from spontaneous response fluctuation while subjects fixate at uniform gray background or keep their eyes closed.

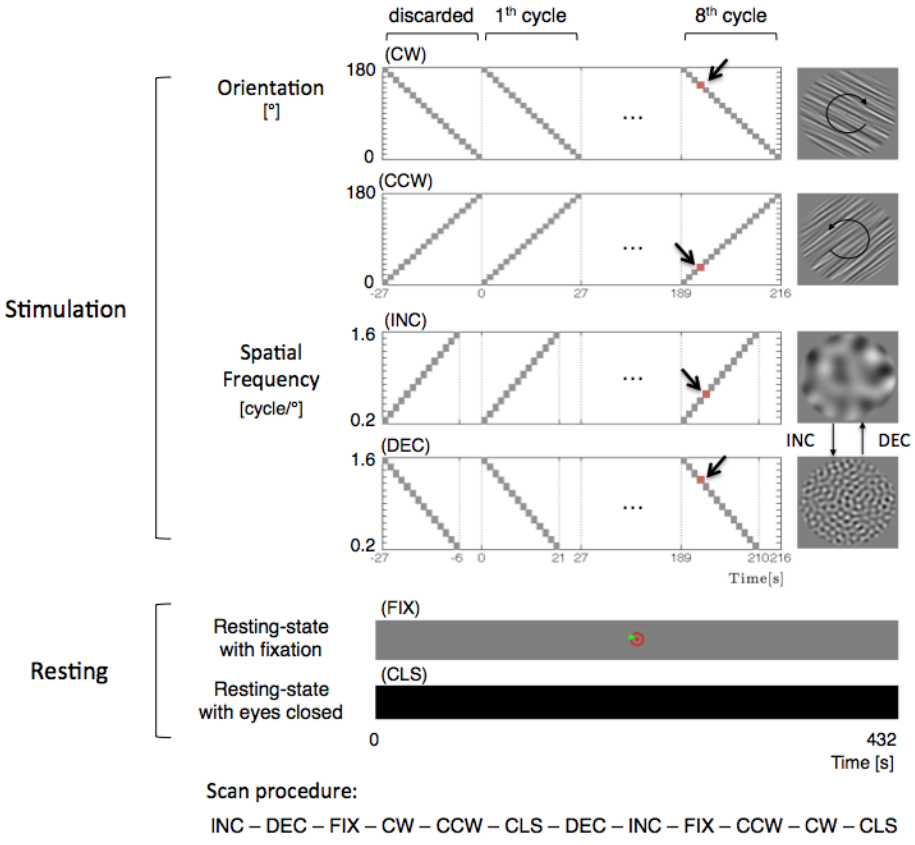

Figure 7. Stimuli and scan structures for fMRI data collection

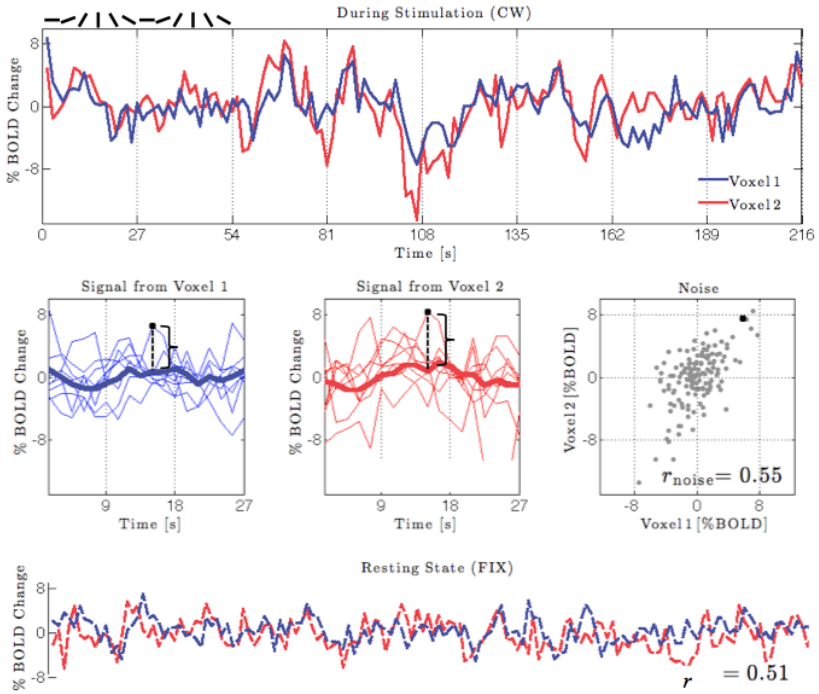

Figure 8. Definition of driven-state and resting-state responses

Results and Discussion.

Trial-by-trial fMRI BOLD measurements were largely positively correlated between voxels, consistently in the areas we studied and their both hemispheres. As an initial step in searching for the structure of noise correlation, we first sorted out voxel pairs depending on their relative RF positions in visuotopic space defined by polar coordinates. Noise correlation was relatively high for the voxel pairs whose RFs fall upon the same polar angle axis or the same eccentricity axis (Fig. 9).

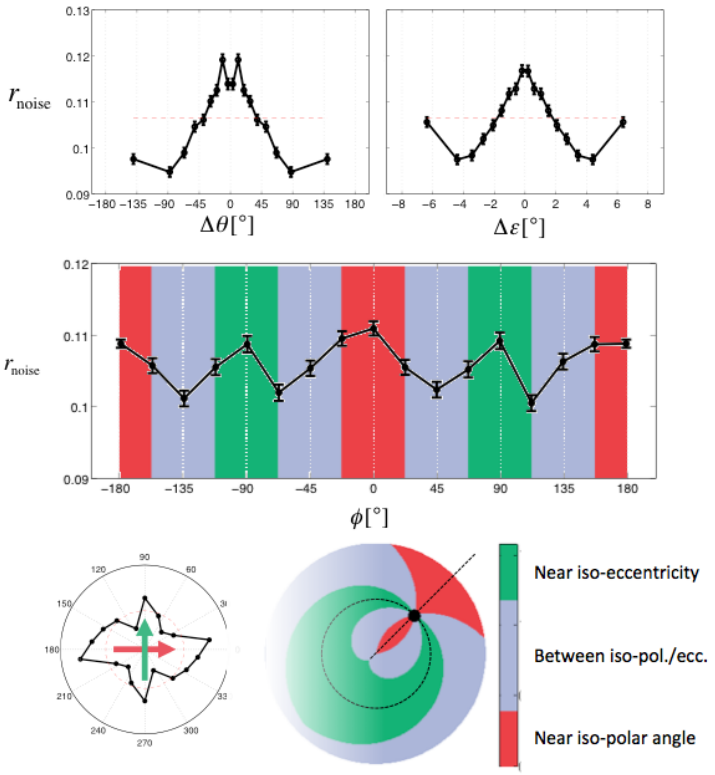

Figure 9. Anisotropy in noise correlation along polar-angle and eccentricity axes in visuotopic space

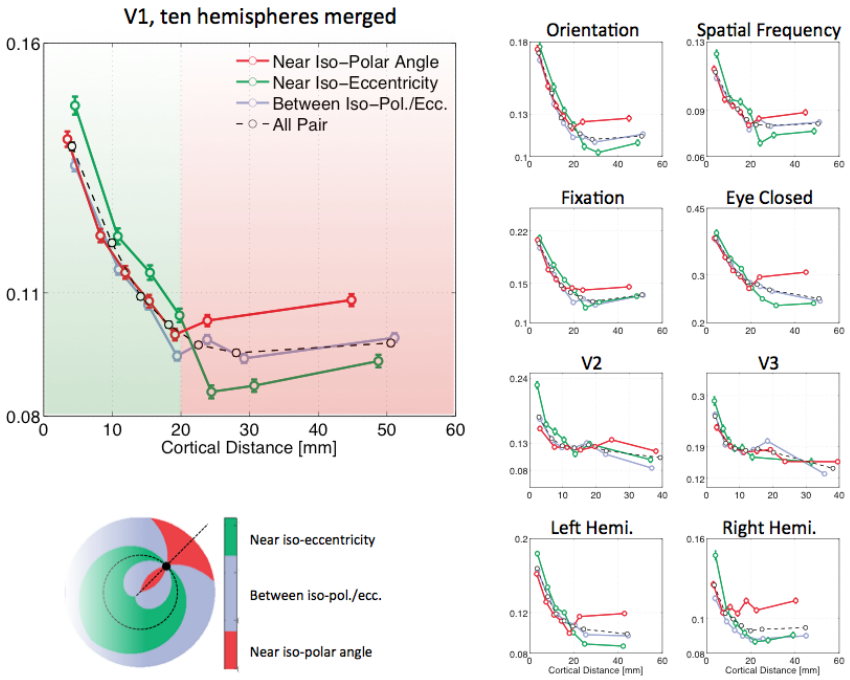

Figure 10. Anisotropy in noise correlation over cortical surface

To further specify the anisotropic spread of noise correlation over cortical surface, we measured how noise correlation varies as a function of cortical distance (Fig. 10). Not surprisingly, noise correlations steadily decreased with increasing cortical distance, dropping to almost a half when voxel pairs were 15mm apart in V1. Most intriguingly, at the short cortical distance regime (less than 20mm), the noise correlation was high between voxels with RFs sharing the same eccentricity (concentric) axis in visuotopic space. In contrast, at the long cortical distance regime (more than 20mm), the highest correlation was found in the voxel pairs whose RFs share the iso-polar-angle (radial) axis. This distance-dependent spatial anisotropy in noise correlation holds true irrespective of the stimulus

types (frequency-filtered orientation-filtered images) and input stimulus regimes (stimulus & fixation, fixation, or eye-closed), even though the overall level of noise correlation tended to increase from the stimulus & fixation condition, to the fixation condition, and to the eye-closed condition.

Our findings suggest that the anisotropy in noise correlation found in the current study is likely to reflect the 'intrinsic' bias in connectivity built in between local sites in the early visual cortex, implying a corresponding bias in cortical processing of visual input.

List of Publications and Significant Collaborations that resulted from your AOARD supported project: In standard format showing authors, title, journal, issue, pages, and date, for each category list the following:

b) papers published in peer-reviewed conference proceedings,

Kyoung whan Choe, Randolph Blake, and Sang-Hun Lee. Decomposition of stimulus representations and decision-bias signatures in population activity of human primary visual cortex. Journal of Vision, 2013, 13(9): 1264; doi:10.1167/13.9.1264

c) papers published in non-peer-reviewed journals and conference proceedings,

Jungwon Ryu and Sang-Hun Lee. Intrinsic Bias in Functional Connectivity in the Early Visual Cortex Evidenced by Driven and Spontaneous fMRI Measurements from Humans. Korean conference on brain and cognitive sciences. September, 2013, Seoul, Korea.

Jungwon Ryu and Sang-Hun Lee. Principal Component Analysis of fMRI measurements from Human Early Visual Cortex Reveals a Robust Structure of Variability Common to Spontaneous and Driven Cortical Population Activity. Korean conference on brain and cognitive sciences. September, 2013, Seoul, Korea.

e) manuscripts submitted but not yet published,
Kyoung whan Choe, Randolph Blake, and Sang-Hun Lee. Dissociation between Neural Signatures of Stimulus and Choice in Population Activity of Human V1 during Perceptual Decision Making. The Journal of Neuroscience (submitted, reviewed, now under revision).

Attachments:

Three files (1 b & 2 c) are attached.

DD882: As a separate document, please complete and sign the inventions disclosure form.